LIGAND GENES AND THEIR USE FOR IMMUNOMODULATION AND TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES Inventor(s): Thomas Kipps, et al.; Serial No.: 08/982,272 Filing Date: December 1, 1997; Atty. Docket No.: 041673-2069 Π 330 786 Ш mCD40L 783 III bovCD40L 786 Ш 11 IV hTNF-α 168 699 SEP 3 0 21.93 Ш 11 IV mTNF-α 11 Ш I۷ pigTNF-α 168 Ш IV 11 hTNF-β Ш 11 IV pigTNF-β 126 150 612 Π Ш IV hFasL 843 11 Ш IV mFasL 309 237 384 837 11 Ш IV hCD70 117 132 579 11 III IV mCD70 123 138 585 11 III IV hCD30L 186 11 Ш IV h4-1BBL DOMAINS: I - Cytoplasmic Domain; II - Transmembrane Domain; III - Proximal Extracellular Domain; IV - Distal Extracellular Domain (putative soluble form)

NOVEL EXPRESSION VEGTORS CONTAINING ACCESSORY MOLECULE

Figure 1



င် ჯ Σ ₽ ₽ CD40 Ξ K Ж Ä CHIMERIC **EXCHANGE** ჯ MOUSE CD40L; EXPRESSION (+) HUMAN CD40L; EXPRESSION (-) ₽ 띴 Ξ

Figure 2



Figure 3



NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MOLECULE LIGAND GENES AND THEIR USE FOR IMMUNOMODULATION AND TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES Inventor(s): Thomas Kipps, et al.; Serial No.: 08/982,272

Filing Date: December 1, 1997; Atty. Docket No.: 041673-2069

NONINFECTED

+mCD40-L ADENOVIRUS

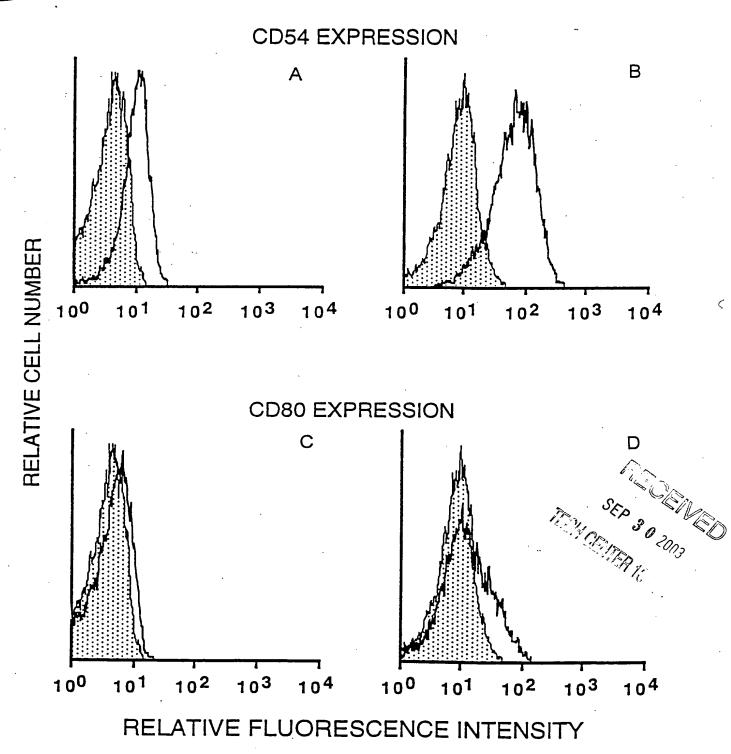


Figure 4



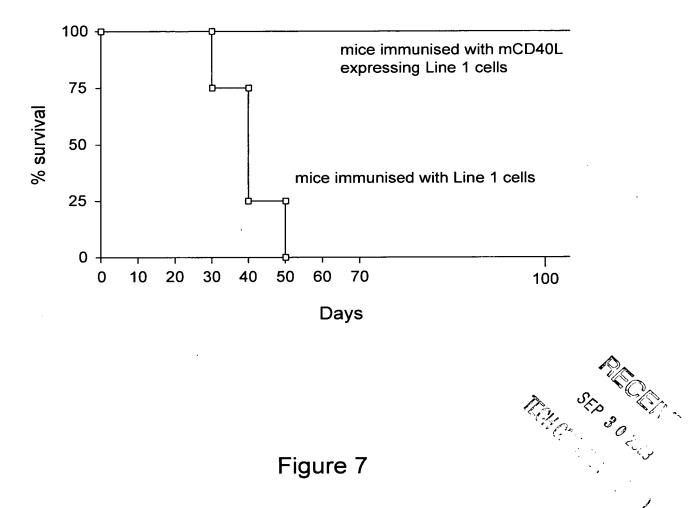
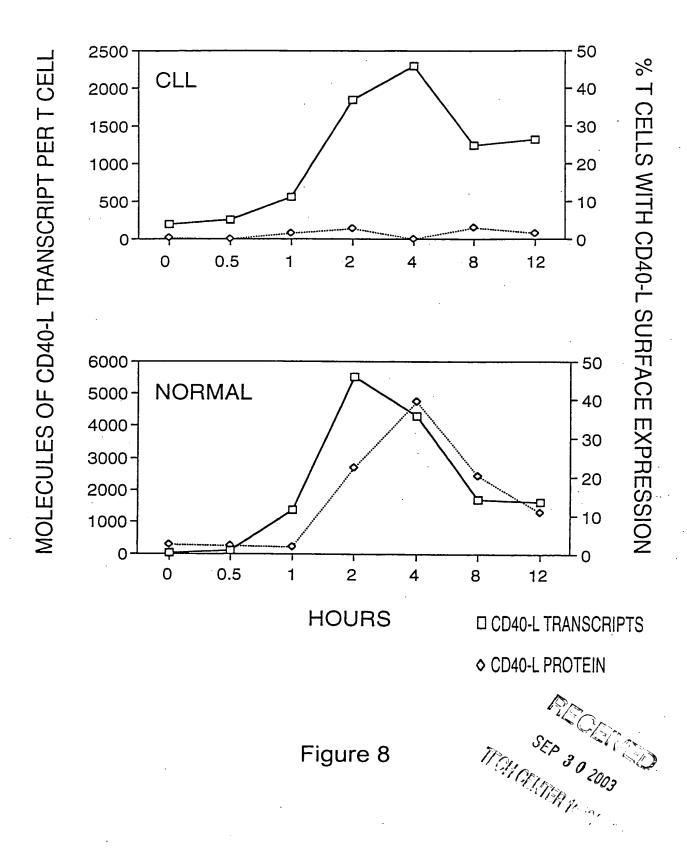
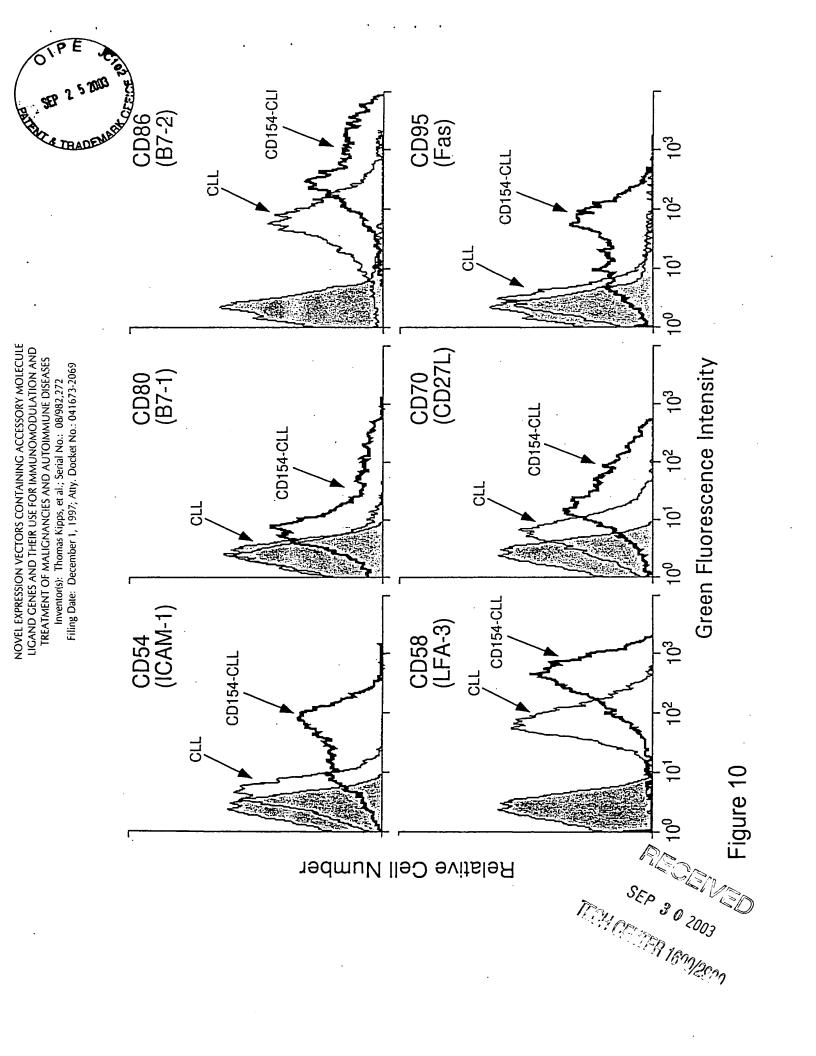
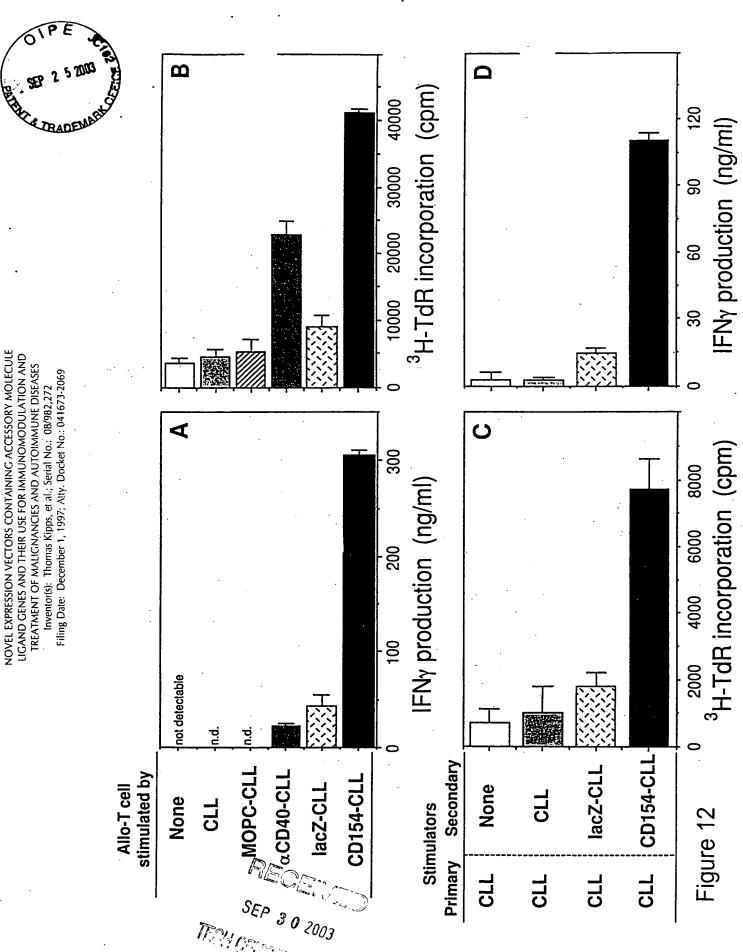


Figure 7









TRONG TO A

Filing Date: December 1, 1997; Atty. Docket No.: 041673-2069 Inventor(s): Thomas Kipps, et al.; Serial No.: 08/982,272



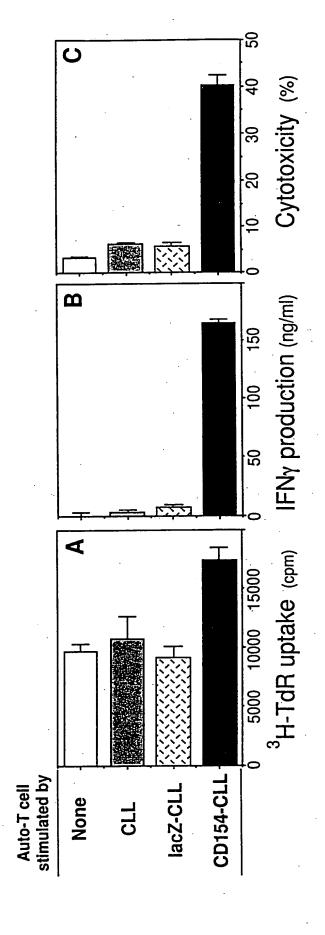
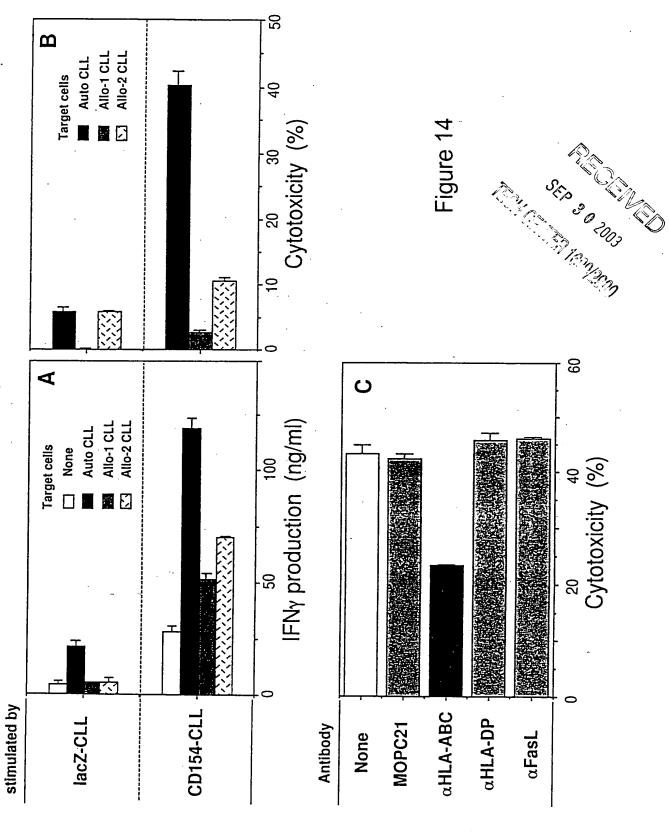


Figure 13



T cell



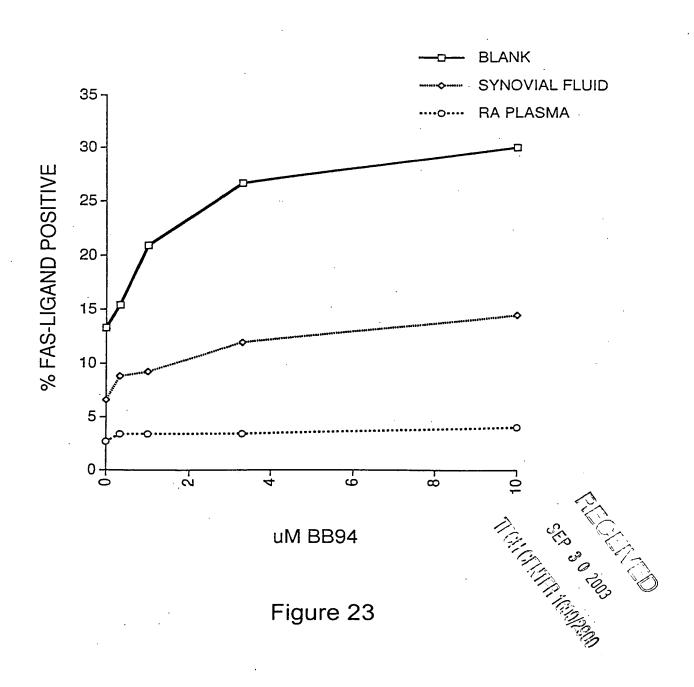


Relative Cell Number

Figure 15

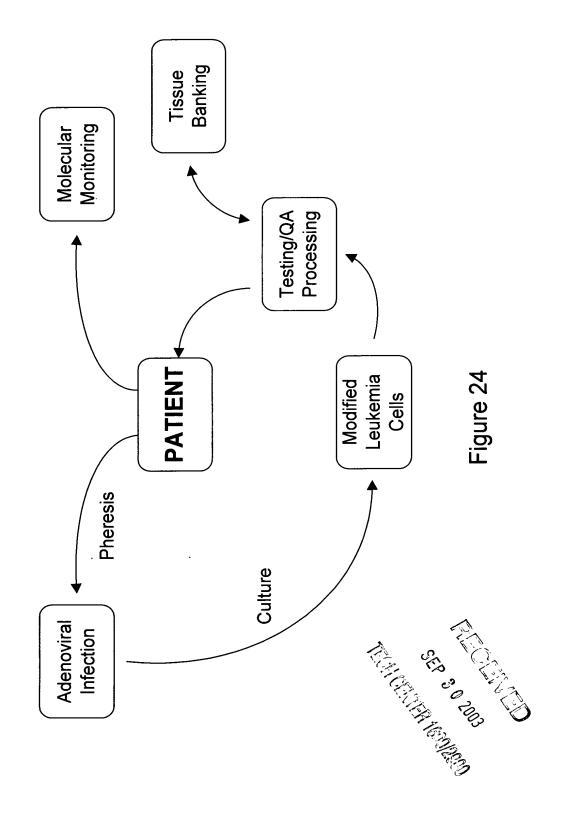


RA SYNOVIAL FLUID AND PLASMA INHIBITION OF FAS-LIGAND





Gene Therapy of Leukemia



Matrix Metalloproteinase Cleavage Sites

		NOVEL E LIGAND TREAT I I Filing	XPRESSION VECTORS CO GENES AND THEIR USE I MENT OF MALIGNANCIE Iventor(s): Thomas Kipps, 3 Date: December 1, 1997	NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MOLECULE LIGAND GENES AND THEIR USE FOR IMMUNOMODULATION AND TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES Inventor(s): Thomas Kipps, et al.; Serial No.: 08/982,272 Filing Date: December 1, 1997; Atty. Docket No.: 041673-2069	ON ECULE ON AND SEASES 72 -2069		ENT & TEL
SER 30 2003	SE CO	Matri	x Metalloprote	Matrix Metalloproteinase Cleavage Sites	je Sites		DEMARKO
		Cleavage <u>∥</u>					•
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Collag	Collagenases					·	
MMP-1	Interstitial	Interstitial Collagenase					
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Glv/Leu	OLL Ten	Leu Met/Tvr	S E	Met	Arg eu	Met/Ala	Arg '
Met		Val/Gly	oli Oli		Phe	Çiğ Xəf	s le
Olu	Asp	, e	Tyr	Gln	Tro	Ser	<u> </u>
Pro		Gln/Arg	Aja	Pro	Bln	: 5	2 €
Tyr		Asp	Phe	Phe	Ala	Phe	Ser
<u>е</u>		Olu	Glu	Ala	Val/Gly	Arg	ng G
Th		Ala	Asn	Tyr/Val	Ser	Pro	Ala
Arg		.*		[not K,E,W]	Asn		
		:					
AIMF-8	Neutrophil	Neutrophil Collagenase					
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Ala Ol.		ren	Olu Olu	Туг	Ala	Gly	Arg
Gly/Leu		Gln	Gly/His	<u>le</u>	ren Len	Met	GIn
Met			Ala	Leu	Trp	Ala	
<u>n</u> g (Val			
Pro				Phe	-		
Tyr/lle/Thr/Arg	hr/Arg		Ala		H.	Figure 28A	
(otherwi	(otherwise same as MMP-1)	P-1)	٠	-	-		

NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MOLECULE LIGAND GENES AND THEIR USE FOR IMMUNOMODULATION AND TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES Inventor(s): Thomas Kipps, et al.; Serial No.: 08/982,272 Filing Date: December 1, 1997; Atry. Docket No.: 041673-2069

Gelatinases	ses						
MMP-2	Gelatinase A						
₫,	ሚ		ፈ	ā.	P,	P.	ŗ
Gly	Pro		Gly	Leu	Ala/Leu	Gly/Ala	Gin
· ·	Ala		Asn	lle/Phe	Phe/Trp	Ľeu	Arg
Pro	Arg		Ala	Val/Met	Gly	Ser	. 왕
Arg			His	Ala	Arg/Gln	Pro	Pro
Leu		Lys	Leu	Glu	His		
		lle	Tyr	Gln/Asn	Val		
		His		Ser	• .		
MMD_0	Golatinase B						
	סכומנווומאל ט		٥	Ĝ	à	ā	Ĉ
-	P. 0		<u>. </u>		- Z	Γ3 <u>Α</u> Ι3	r 1-
) : :		5	lle/Phe	Ala/Leu/Phe	Leu	=
Gln/Arg							
-		Leu		Val/Met	Trp/Gly	Ser	
				Ala		Gly	
Stromelysir	/sins						
MMP-3	melysin						
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Asp	Pro	Phe		Leu	Arg	Ala	重
Gly	Ala	Leu/Met		Phe	Leu/Phe	Arg/Met	
Gln/Arg							
Leu	Val	Tyr		Trp/Tyr	Trp	Gly	Pro
<u>e</u>		Pro/Gly/Glu		<u>e</u>	Val	Val/Ile	
Glu/Val							
Leu		lle		Val	Gln	Ser/Asn	Ala
Lys		Ala		Met	His/Met	Glu/Thr	
Gly/Asp							
Arg	Arg	Ser	Leu/Pro	Glu	Glu/Ser/Thr	Leu	
Ser/Lys/Phe							
Pro/Met	Ser/Gly		Lys/Tyr/Arg				
Ala/Phe/Gl	u				-		

Figure 28B

NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MOLECULE LIGAND GENES AND THEIR USE FOR INMUNOMODULATION AND TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES Inventor(s): Thomas Kipps, et al.; Serial No.: 08/982,272 Filing Date: December 1, 1997; Atty. Docket No.: 041673-2069

OIPE CO	S. C.
REAL TRADENAN	ė

₽ Q ∢	a. Ø
P ,3 Ala Glu	P' , Ala Val/Arg/Met Gly
P , Gn Val	P' Arg Met Gin
P, le Leu	P , Leu Met
P. His Leu	P. Glu Met/Ala Pro/Gln Gly
F His	P₂ Leu Gln Val
Stromelysin 2 · P ₃ Ala Pro	Matrilysin P ₃ Pro Leu
MMP-10 P ₄ Arg Gly	Others MMP-7 P ₄ Ile Gly Pro

Figure 28C